

REMARKS

Status of the Claims

Pending claims

Claims 21 to 33 are pending and under consideration.

Allowed claims

Applicants thank the Examiner for finding that claim 21 is allowable.

Response to the Restriction Requirement

In response to the Restriction Requirement mailed February 12, 2001, Applicants elected a sequence as set forth in SEQ ID NO:23, with traverse.

Claims amended, canceled, and added in the instant amendment

In the present Response, claims 22 to 25 are canceled; claims 21, 26, 27, 32 and 33 are amended; and new claims 34 to 53 are added. Thus, after entry of these amendments, claims 21 and 26 to 53 are pending and under consideration.

Outstanding Rejections

Pursuant to the instant Office Action, claims 22 to 33 are rejected under 35 U.S.C. §112, second paragraph. Claims 22 to 33 are rejected under 35 U.S.C. §112, first paragraph. Applicants respectfully traverse all outstanding rejections of the claims.

Support for the Claim Amendments

Support for the new and amended claims can be found throughout the application for the skilled artisan. For example, support for claims directed to oligonucleotide probes that hybridize under specific conditions can be found, inter alia, page 9, line 24, to page 10, line 6, of the specification. Claims directed to use of oligonucleotide probes of specific lengths can be found, inter alia, on page 12, third paragraph, and page 13, second and third full paragraphs. Claims directed to use of oligonucleotide probes as amplification primers or diagnostic probes can be found, inter alia, on page 13, second full paragraph, and, page 26, first paragraph, and page 28, Example 2. Applicants submit that no new matter is introduced by the instant amendment.

Issues under 35 U.S.C. §112, second paragraph

Claims 22 to 33 are rejected under 35 U.S.C. §112, second paragraph, for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regards as the invention.

The phrase "comprising a nucleic acid sequence consisting of a sequence..."

The Patent Office alleges that claim 26 is confusing in the recitation of "comprising a nucleic acid sequence consisting of a sequence..." because of the combination of the open language of the term "comprising" with the closed language of the term "consisting of." The instant amendment addresses this issue.

The term "stringent conditions"

The Patent Office alleges that claim 26 is indefinite in the recitation of "stringent conditions." The instant amendment addresses this issue.

The phrase "specifically hybridizes to a nucleic acid ..."

The Patent Office alleges that claim 27 is indefinite in the recitation of "specifically hybridizes to a nucleic acid having at least 95% identify to SEQ ID NO:23." The instant amendment addresses this issue.

In light of the foregoing amendments and remarks, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 22-33 based upon 35 U.S.C. §112, second paragraph.

Issues under 35 U.S.C. §112, first paragraph

Written Description

The Patent Office alleges that the specification does not contain any disclosure of the structure and function of the genus of oligonucleotide probes which comprise a sequence which specifically hybridizes to SEQ ID NO:23, its complement or to a nucleic acid having 95% identity thereto. It is alleged that claims directed to a genus of probes are not described in the

specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s) at the time the application was filed, had possession of the claimed invention.

Applicants respectfully submit that the claimed invention is sufficiently described in the specification so that one of ordinary skill in the art would be able to ascertain the scope of the claims with reasonable clarity and recognize that Applicants' were in possession of the claimed invention at the time of filing. Applicants respectfully aver that describing a genus of polynucleotides in terms of its physico-chemical properties (e.g., specific stringent conditions) and function (e.g., binding to/ detecting an esterase-encoding nucleic acid, or its complement) satisfies the written description requirement of section 112, first paragraph.

Applicants respectfully refer to the USPTO guidelines concerning compliance with the written description requirement of U.S.C. §112, first paragraph. In example 14 of the guidelines (a copy of which is attached as Appendix A), a claim reciting variants claimed by sequence identity to a sequence is sought (specifically, "A protein having SEQ ID NO:3 and variants thereof that are at least 95% identical to SEQ ID NO:3 and catalyze the reaction of A → B). In the example, the specification is described as providing SEQ ID NO:3 and a function for the protein. The specification contemplates, but does not exemplify variants of SEQ ID NO:3 that can have substitutions, deletions, insertions and additions (in other words, a genus of polynucleotides). Procedures for making proteins with substitutions, deletions, insertions, and additions are routine in the art and an assay is described which will identify other proteins having the claimed catalytic activity. The analysis of example 14 states that procedures for making variants (which have 95% sequence identity) are conventional in the art. The Guidelines conclusion states that the disclosure meets the requirements of 35 U.S.C. §112, first paragraph, as providing adequate written description for the claimed invention.

Analogously, the claimed nucleic acids are described by structure (the exemplary nucleic acid), a physico-chemical property (e.g., specific hybridization conditions) and function (inter alia, binding to, amplifying, detecting an esterase-encoding nucleic acid, or its complement). The specification discloses specific hybridization conditions that provide the skilled artisan with a physical/chemical property for the claimed oligonucleotides probes. The specification also discloses a function for the claimed oligonucleotides probes. Accordingly, the specification adequately describes the claimed genus of oligonucleotide probes.

The claims fully comply with the requirements for written description of a genus of nucleic acids. In University of California v. Eli Lilly & Co., 43 USPQ2d 1398 (Fed. Cir. 1997), the Federal Circuit stated that, “[a] description of a genus of cDNA may be achieved by means of a recitation of a representative number of cDNAs....*or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus.*” [emphasis added] Lilly, 43USPQ2d at 1406.

As noted above, the instant claims clearly set forth specific structural and physical characteristics of the claimed genus of oligonucleotide probes. The claimed genus of oligonucleotide probes are capable of, inter alia, binding to, detecting, measuring the amount of and/or isolating esterase-encoding nucleic acids. The claimed genus of oligonucleotide probes has a specific physical characteristic, e.g., hybridization under specific conditions, to the exemplary nucleic acid. Therefore, the claimed genus of oligonucleotide probes are defined via shared physical and structural properties in terms that “convey with reasonable clarity to those skilled in the art that Applicant, as of filing date sought, was in possession of invention.” Vas-Cath Inc. V. Mahukar, 19 USPQ2d 1111 (Fed Cir. 1991).

More recently, the Federal Circuit stated

Similarly, in this court's most recent pronouncement, it noted:

More recently, in Enzo Biochem, we clarified that Eli Lilly did not hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written description requirement; rather, the requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure.

Amgen, 314 F.3d at 1332 [Amgen Inc. v. Hoechst Marion Roussel Inc., 314 F.3d 1313, 1330, 65 USPQ2d 1385, 1397 (Fed. Cir. 2003)].

Moba, B.V. v. Diamond Automation, Inc., 2003 U.S. App. LEXIS 6285; Fed. Cir. 01-1063, -1083, April 1, 2003.

Analogously, the disclosed functions of the claimed genus of oligonucleotide probes (e.g., binding to, measuring, isolating and/or detecting an esterase-encoding nucleic acid, or its complement) are sufficiently correlated to a particular, known structure (the exemplary sequence) and a physical (physico-chemical) property (hybridization under specific conditions). Accordingly, the claimed sequences are defined via shared physical and structural properties in

terms that convey with reasonable clarity to those skilled in the art that Applicants, as of the filing date and at the time of the invention, were in possession of the claimed invention.

Applicants also respectfully note that claims directed to a genus of nucleic acids as described and enabled by the specific physical characteristic of stringent hybridization and function have been issuing from the USPTO recently and for many years, see, e.g., U.S. Patent Nos. 6,541,684; 6,541,236; 6,541,220; 6,534,309; 6,492,150; 6,465,210; 6,413,522; 6,384,304; 6,342,657; 6,274,790 (selected claims from these patents are attached as Appendix A).

Accordingly, Applicants respectfully submit that the pending claims meet the written description requirement under 35 U.S.C. §112, first paragraph.

Enablement

The Patent Office notes that the specification enables a probe consisting of a fragment of SEQ ID NO:23 which will hybridize to SEQ ID NO:23 under stringent conditions and optionally a detectable label. However, it is alleged that the specification does not reasonably provide enablement for a genus of oligonucleotide probes which specifically hybridizes to any nucleic acid having 95% identity to SEQ ID NO:23 under any conditions. It is alleged, inter alia, that designing probes which would specifically detect any particular sequence under any conditions would require undue experimentation.

Applicants believe that entry of the instant amendment that modifies claims to expressly contain specific conditions for hybridization addresses the Examiner's concerns.

However, Applicants respectfully maintain that the specification enabled the skilled artisan at the time of the invention to make and use the genus of claimed oligonucleotide probes. The state of the art at the time of the invention and the level of skill of the person of ordinary skill in the art was very high. Hybridization is one of the most basic tools in molecular biology. It is the basis of sequencing, Southern blots, Northern blots, PCR, nucleic acid based screening assays, nucleic acid-based diagnostic assays, to name just a few uses of hybridization.

Applicants respectfully note that routine experimentation in the art includes screening large numbers of nucleic acid sequences. In fact, whether large numbers of compositions (e.g., oligonucleotides, antibodies, proteins) must be screened to determine if one is within the scope of a claimed invention is irrelevant to an enablement inquiry. Enablement is

not precluded by the necessity to screen large numbers of compositions, as long as that screening is "routine," i.e., not "undue," to use the words of the Federal Circuit. The Federal Circuit in *In re Wands* directed that the focus of the enablement inquiry should be whether the experimentation needed to practice the invention is or is not "undue" experimentation. The court set forth specific factors to be considered.

One of these factors is "the quantity of experimentation necessary." Guidance as to how much experimentation may be needed and still not be "undue" was set forth by the Federal Circuit in, e.g., Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987). An applicant had claims that were generic to all IgM antibodies directed to a specific antigen. However, only a single antibody producing cell line had been deposited. The PTO had rejected claims that were generic to all antibodies directed to the antigen as lacking an enabling disclosure.

The Federal Circuit held that it would not have taken undue experimentation to make and use the claimed invention, where a single deposited antibody producing cell line enabled a claim generic to all IgM antibodies directed to a specific antigen. The Federal Circuit noted that the evidence indicated that those skilled in the monoclonal antibody art could, using the state of the art and applicants' written disclosure, produce and screen new hybridomas secreting other monoclonal antibodies falling within the genus without undue experimentation. The court held that applicants' claims need not be limited to the specific, single antibody secreted by the deposited hybridoma cell line (significantly, the genus of antibodies was allowed even though only one antibody specie was disclosed). The court was acknowledging that, because practitioners in that art are prepared to screen large numbers of negatives in order to find a sample that has the desired properties, the screening that would be necessary to make additional antibody species was not "undue experimentation."

Analogously, practitioners of the biological sciences for the instant invention also recognize the need to screen large numbers of negatives to find a sample that has the desired properties, e.g., oligonucleotide probes that hybridize to esterase-encoding nucleic acids under specific conditions. Furthermore, the screening procedures used to identify oligonucleotide probes within the scope of the instant invention were all well known in the art at the time of the invention. These screening procedures were routine protocols for the skilled artisan at the time

of the invention. Thus, the skilled artisan using Applicants' written disclosure could practice the claimed invention without undue experimentation.

The instant specification provided exemplary oligonucleotide probes which one of ordinary skill in the art could use and manipulate to practice the full scope of the claimed invention. The specification provided the skilled artisan with specific hybridization conditions (see, e.g., the paragraph spanning pages 9 and 10). The specification provided exemplary methods for using oligonucleotides (e.g., as amplification primers) to identify and make esterase-encoding nucleic acids (see, e.g., Examples 1 and 2, pages 26 to 28). The specification provided an exemplary esterase activity assay (see, e.g., Example 4, pages 29 to 30). Esterase activity also could have been determined by routine experimentation using protocols well known at the time of the invention. Accordingly, Applicants respectfully submit that the specification reasonably enabled one of ordinary skill in the art to make and use the claimed invention at the time of the invention.

Applicants also respectfully note that claims directed to a genus of nucleic acids as described and enabled by the specific physical characteristic of stringent hybridization and function have been issuing from the USPTO recently and for many years, see, e.g., U.S. Patent Nos. 6,541,684; 6,541,236; 6,541,220; 6,534,309; 6,492,150; 6,465,210; 6,413,522; 6,384,304; 6,342,657; 6,274,790 (selected claims from these patents are attached as Appendix A).

CONCLUSION

Applicants request that the Examiner reconsider the application and claims in light of the foregoing reasons and amendments and respectfully submit that the claims are in condition for allowance.

If, in the Examiner's opinion, a telephonic interview would expedite the favorable prosecution of the present application, the undersigned attorney would welcome the opportunity to discuss any outstanding issues and to work with the Examiner toward placing the application in condition for allowance.

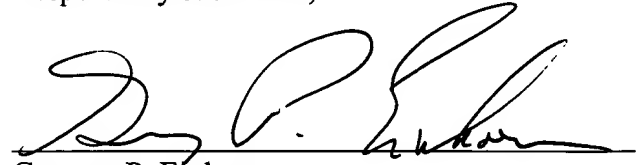
Applicant : Robertson, et al.
Serial No. : 09/382,242
Filed : August 22, 1999
Page : 14 of 14

Attorney's Docket No.: 09010-010002 / DIVER1180

Applicants believe that no additional fees are necessitated by the present Response. However, in the event any such fees are due, the Commissioner is hereby authorized to charge any such fees to Deposit Account No. 06-1050.

Respectfully submitted,

Date: May 9, 2003


Gregory P. Einhorn
Reg. No. 38,440

Fish & Richardson P.C.
4350 La Jolla Village Drive, Suite 500
San Diego, California 92122
Telephone: (858) 678-5070
Facsimile: (858) 678-5099

Applicant : Robertson, et al.
Serial No. : 09/382,242
Filed : August 22, 1999
Title : ESTERASES

Art Unit : 1652
Examiner : Rebecca E. Prouty, Ph.D.

APPENDIX A

Nucleotide sequences encoding maize RAD51

Abstract

Nucleic acid sequences encoding two RAD51 recombinases active in maize plants are provided. cDNA sequences including the ZmRAD51 coding sequences and unique 3'-untranslated regions which are useful as RFLP probes, are also provided. The production of plasmids containing a nucleic acid sequence encoding a ZmRAD51 fusion protein, as well as the use of the plasmids to introduce the ZmRAD51 coding sequence into a host cell, such as maize cell, are also disclosed.

Inventors: **Bowen; Benjamin A.** (Hayward, CA); **Chamberlin; Mark A.** (Windsor Heights, IA); **Drummond; Bruce J.** (Des Moines, IA); **McElver; John A.** (Durham, NC); **Rothstein; Rodney J.** (Maplewood, NJ)

Assignee: **Trustees of Columbia University in the City of New York** (New York, NY); **Pioneer Hi-Bred International, Inc.** (Johnston, IA)

Appl. No.: **246963**

Filed: **February 9, 1999**

Current U.S. Class: 800/320.1; 435/69.1; 435/196; 536/23.1; 536/23.5;
536/24.1

Intern'l Class: A01H 005/00

Field of Search: 536/23.1,23.5,24.1 435/410,468,196,69.1
800/298,320.1

References Cited [Referenced By]

Foreign Patent Documents

WO 93/22443	Nov., 1993	WO.
WO 97/41228	Nov., 1997	WO.

Other References

Natalie Teager et al, Isolation and characterization of rad51 orthologs from *Coprinus cinereus* and *Lycopersicon esculentum*, and phylogenetic analysis of eukaryotic recA homologs, *Curr Genet* 1997, 31: 144-157.*
Kowalczykowski, et al. 1994. Homologous Pairing and DNA Strand-Exchange Proteins. *Annu Rev. Biochem.* 1994. 63:991-1043.
Sung, 1994. Catalysis of ATP-Dependent Homologous DNA Pairing and Strand

Exchange by Yeast RAD51 Protein. Science, vol. 265, 1241-1243.
Stassen, et al. Isolation and characterization of rad51 orthologs from Coprinus cinereus and Lycopersicon esculentum, and phylogenetic analysis of eukaryotic recA homologs. Curr Genet (1997) 31: 144-157.
Doutriaux, et al. Isolation and characterisation of the RAD51 and DMC1 homologs from Arabidopsis thaliana. Mol Gen. Genet (1998) 257: 283-291.
Kanaar and Hoeijmakers, 1998. From competition to collaboration. Nature, vol. 391, 335-338.
Benson, et al. 1998. Synergistic actions of Rad51 and Rad52 in recombination and DNA repair. Nature, vol. 391, 401-404.
Shinohara and Ogawa, 1998. Stimulation by Rad52 of yeast Rad51-mediated recombination. Nature, 391: 404-407.
New, et al., 1998. Rad 52 protein stimulates DNA strand exchange by Rad51 and replication protein A. Nature, 391: 407-410.
Smith, K.N., et al. 1996. Untitled. Embl. Sequence Data Library, XP002105502, Accession No. U43528.

Primary Examiner: Ketter; James
Attorney, Agent or Firm: Foley & Lardner

Parent Case Text

CROSS REFERENCE TO RELATED APPLICATION

This application claims the benefit of U.S. Provisional Application No. 60/074,745, filed Feb. 13, 1998 and is herein incorporated by reference.

Claims

What is claimed is:

1. An isolated polynucleotide comprising a member selected from the group consisting of:
 - a) a polynucleotide encoding a polypeptide selected from the group consisting of SEQ ID NO: 3 and SEQ ID NO: 7;
 - b) a polynucleotide having at least 90% identity to a polynucleotide of (a);
 - c) a polynucleotide which will hybridize under ***stringent hybridization*** conditions to said polynucleotide of (a) or (b); and

d) a polynucleotide comprising at least 30 contiguous nucleotides from a polynucleotide of (a), (b) or (c);

wherein the polynucleotide of (a), (b) or (c) encodes a polypeptide with recombinase activity.

2. The isolated polynucleotide of claim 1, wherein said polynucleotide has a sequence selected from the group consisting of SEQ ID NO: 2 and SEQ ID NO: 6.

3. An expression cassette comprising a polynucleotide of claim 1 operably linked to a promoter.

4. The host cell transfected with an expression cassette of claim 3.

5. The host cell of claim 4, wherein said host cell is a bacterial cell.

6. The host cell of claim 4, wherein said host cell is a sorghum or maize cell.

7. A method of making maize recombinase comprising the steps of:

a) transforming or transfecting a host cell with the expression cassette of claim 3; and

b) purifying the recombinase from the host cell.

8. The method of claim 7, wherein the host cell is selected from the group consisting of a bacterial cell, a plant cell, a mammalian cell and a yeast cell.

9. A method of modulating ZmRAD 51 activity in a plant, comprising:

(a) introducing into a plant cell an expression cassette comprising an isolated polynucleotide of claim 1 operatively linked to a promoter;

(b) culturing the plant cell under plant cell growing conditions;

(c) regenerating a plant which possesses the transformed genotype, and

(d) inducing expression of said polynucleotide for a time sufficient to modulate ZmRAD51 activity in said plant.

10. A transgenic plant cell comprising an isolated polynucleotide of claim 1.

11. A transgenic plant comprising an isolated polynucleotide of claim 1.

12. A transgenic seed from the transgenic plant of claim 11.

13. Primer pairs for isolating at least a part of a Zea mays recombinase gene, selected

Protein having glutaminase activity and gene encoding the same

Abstract

There are disclosed a protein having an amino acid sequence represented by amino acid numbers 1 to 684 or 49 to 684 shown in SEQ ID NO:2, or a protein having a glutaminase activity in which one or more amino acids is/are deleted from, substituted by, inserted to or added to the amino acid sequence of the above protein; a gene containing DNA encoding the above protein or a gene encoding a protein which hybridizes with the DNA of the above gene under a stringent condition and has a glutaminase activity; a recombinant DNA containing the above gene; a transformant or a transductant containing the above recombinant DNA; and a process for producing glutaminase which comprises culturing the above transformant or the above transductant and collecting glutaminase from a culture medium.

Inventors: **Ito; Kotaro** (Noda, JP); **Umitsuki; Genryou** (Noda, JP); **Koyama; Yasuji** (Noda, JP)

Assignee: **Kikkoman Corporation** (Chiba-ken, JP)

Appl. No.: **946678**

Filed: **September 6, 2001**

Foreign Application Priority Data

Sep 06, 2000[JP]	2000-270371
Current U.S. Class:	435/227; 435/320.1; 435/223.2; 435/440; 435/6; 435/252.3; 536/23.2
Intern'l Class:	C12N 009/78; C12N 015/00; C12N 001/20; C07H 021/04
Field of Search:	435/227,320.1,257.3,232.2,440,6,272.2 536/23.2

References Cited [Referenced By]

U.S. Patent Documents			
<u>6063409</u>	May., 2000	Sato et al.	426/52.
Foreign Patent Documents			
A11332553	Dec., 1999	JP.	

Other References

Huser et al. Cloning, sequence analysis, and expression of ansB from *Pseudomonas fluorescens*, encoding periplasmic glutaminase/asparaginase. FEMS Microbiol Lett. 15;178 (2);327-335. Sep. 1999.

Primary Examiner: Achutamurthy; Ponnathapu

Assistant Examiner: Pak; Yong

Attorney, Agent or Firm: Birch, Stewart, Kolasch & Birch, LLP

Claims

What is claimed is:

1. An isolated nucleic acid comprising a nucleotide sequence selected from the group consisting of:

(a) a nucleotide sequence encoding an amino acid sequence comprising amino acids 1 to 634 of SEQ ID NO:2, and

(b) a nucleotide sequence, the complement thereof which binds to said nucleotide sequence (a) under ***stringent hybridization*** conditions of a sodium concentration of 50-300 mM and a temperature of 42-68.degree. C., wherein said nucleic acid encodes a protein having glutaminase activity.

2. An isolated nucleic acid comprising a nucleotide sequence selected from the group consisting of:

(a) a nucleotide sequence encoding an amino acid sequence comprising amino acids 49 to 684 of SEQ ID NO:2, and

(b) a nucleotide sequence, the complete complement thereof which binds to said nucleotide sequence (a) under ***stringent hybridization*** conditions of a sodium concentration of 50-300 mM and a temperature of 42-68.degree. C.,

wherein said nucleic acid encodes a protein having glutaminase activity.

3. An isolated nucleic acid comprising a nucleotide sequence of SEQ ID NO:1, or a complete complement thereof which binds to SEQ ID NO:1 under ***stringent hybridization*** conditions of a sodium concentration of 50-300 mM and a temperature of 42-68.degree. C.,

wherein said nucleic acid encodes a protein having glutaminase activity.

4. A recombinant nucleic acid comprising the nucleotide sequence of claim 3.

Nucleic acid encoding PTH1R receptor

Abstract

The present invention relates to novel parathyroid hormone (PTH) and parathyroid hormone related protein (PTHrP) receptors (PTH1R and PTH3R) isolated from zebrafish. The receptors of the present invention share homology with previously identified parathyroid hormone (PTH)/parathyroid related protein (PTHrP) receptors. Isolated nucleic acid molecules are provided encoding the zebrafish PTH1R and PTH3R receptors. PTH1R and PTH3R receptor polypeptides are also provided, as are vectors, host cells and recombinant methods for producing the same. The invention further relates to screening methods for identifying agonists and antagonists of PTH1R and PTH3R receptor activity and to diagnostic and therapeutic methods.

Inventors: **Juppner; Harald** (Cambridge, MA); **Rubin; David A.** (Needham, MA)

Assignee: **The General Hospital Corporation** (Boston, MA)

Appl. No.: **449632**

Filed: **November 30, 1999**

Current U.S. Class: 435/69.1; 536/23.5; 536/24.3; 536/24.31; 530/350;
435/71.1; 435/71.2; 435/471; 435/325; 435/320.1;
435/252.3; 435/254.11

Intern'l Class: C12N 015/12; C12N 015/63; C12N 005/10; C07K
014/705

Field of Search: 536/23.1,23.5,24.3,24.31 530/350
435/69.1,71.1,71.2,471,325,252.3,254.11,320.1

References Cited [Referenced By]

U.S. Patent Documents

<u>4423037</u>	Dec., 1983	Rosenblatt et al.	424/177.
<u>5010010</u>	Apr., 1991	Gautvik et al.	435/252.
<u>5208041</u>	May., 1993	Sindrey	424/562.
<u>5496801</u>	Mar., 1996	Holthuis et al.	514/12.
<u>5616560</u>	Apr., 1997	Geddes et al.	514/12.
<u>5693616</u>	Dec., 1997	Krstenaansky et al.	514/12.
<u>5695955</u>	Dec., 1997	Krstnenansky et al.	435/69.
<u>5798225</u>	Aug., 1998	Krstenansky et al.	435/69.
<u>5814603</u>	Sep., 1998	Oldenburg et al.	514/17.

Terminus Limit the Response of the Parathyroid Hormone (PTH) 2 Receptor to PTH-related Peptide," J. Biol. Chem. 273:3830-3837 (Feb. 1998).
International Search Report for International Application No. PCT/US99/28207,
mailed Apr. 18, 2000.

Primary Examiner: Mertz; Prema

Attorney, Agent or Firm: Sterne, Kessler, Goldstein & Fox PLLC

Government Interests

**STATEMENT AS TO RIGHTS TO INVENTIONS MADE UNDER FEDERALLY-
SPONSORED RESEARCH AND DEVELOPMENT**

Part of the work performed during development of this invention utilized U.S.
Government funds. The U.S. Government has certain rights in this invention.

Parent Case Text

This application claims the benefit of the filing date of provisional application No.
60/110,467 filed on Nov. 30, 1998, which is herein incorporated by reference.

Claims

What is claimed is:

1. An isolated nucleic acid molecule comprising a polynucleotide having a nucleotide
sequence selected from the group consisting of:

(a) a nucleotide sequence encoding a parathyroid hormone (PTH)/PTH-related peptide
(PfHrP) receptor (PTH1R receptor) having the complete amino acid sequence of amino
acids 1 to 536 in SEQ ID NO:2;

(b) a nucleotide sequence encoding the PTH1R receptor having the amino acid sequence
of amino acids 2 to 536 in SEQ ID NO:2;

(c) a nucleotide sequence encoding the mature PTH1R receptor having the amino acid
sequence of amino acids 25 to 536 in SEQ ID NO:2;

(d) a nucleotide sequence encoding the PTH1R receptor having the complete amino acid
sequence encoded by the cDNA clone deposited with the ATCC as deposit PTA-916;

(e) a nucleotide sequence encoding the mature PTH1R receptor having the amino acid sequence encoded by the cDNA deposited with the ATCC as deposit PTA-916;

(f) a nucleotide sequence encoding the PTH1R extracellular domain, said extracellular domain having the amino acid sequence of amino acids 25 to 147 in SEQ ID NO:2;

(g) a nucleotide sequence encoding the PTH1R transmembrane domain, said transmembrane domain having the amino acid sequence of amino acids 148 to 416 in SEQ ID NO:2; and

(h) a nucleotide sequence complementary to any of the nucleotide sequences in (a), (b), (c), (d), (e), (f) or (g).

2. The nucleic acid molecule of claim 1 wherein said polynucleotide has the complete nucleotide sequence of the cDNA clone deposited with the ATCC as deposit PTA-916.

3. The nucleic acid molecule of claim 1 wherein said polynucleotide has the nucleotide sequence encoding the PTH1R receptor having the complete amino acid sequence encoded by the cDNA deposited with the ATCC as deposit PTA-916.

4. The nucleic acid molecule of claim 1 wherein said polynucleotide has the nucleotide sequence encoding the mature PTH1R receptor having the amino acid sequence encoded by the cDNA clone deposited with the ATCC as deposit PTA-916.

5. An isolated nucleic acid molecule comprising a polynucleotide which hybridizes under **stringent hybridization** conditions to a polynucleotide having a nucleotide sequence identical to a nucleotide sequence in (a), (b), (c), (d), (e), (f), (g) or (h) of claim 1;

wherein said **stringent hybridization** conditions consist of overnight incubation at 42.degree. C. in a solution comprising: 50% formamide, 5.times.SSC (150 mM NaCl, 15 mM trisodium citrate), 50 mM sodium phosphate (pH 7.6), 5.times.Dehardt's solution, 10% dextran sulfate, and 20 g/ml denatured, sheared salmon sperm DNA, followed by washing the filters in 0.1.times.SSC at 65.degree. C.;

wherein said polynucleotide which hybridizes does not have the nucleotide sequence of a human, mouse, rat or bovine PTH1R;

and wherein said polynucleotide which hybridizes does not hybridize under **stringent hybridization** conditions to a polynucleotide having a nucleotide sequence consisting of only A residues or of only T residues.

6. An isolated nucleic acid molecule comprising a polynucleotide which encodes an epitope-bearing region of a PTH1R receptor comprising an amino acid sequence of between 7 and 30 amino acids from the amino acid sequence in (a), (b), (c), (d), (e), (f) or (g) of claim 1.

Motor proteins and methods for their use

Abstract

The invention provides isolated nucleic acid and amino acid sequences of HsKip3d, antibodies to HsKip3d, methods of screening for HsKip3d modulators using biologically active HsKip3d, and kits for screening for HsKip3d modulators.

Inventors: **Beraud; Christophe** (San Francisco, CA); **Freedman; Richard** (San Mateo, CA)

Assignee: **Cytokinetics, Inc.** (South San Francisco, CA)

Appl. No.: **632344**

Filed: **August 3, 2000**

Current U.S. Class: 435/320.1; 435/183; 435/189; 435/252.3;
435/254.11; 435/257.2; 435/325; 536/23.2

Intern'l Class: C07H 021/04; C12N 015/00; C12N 005/00; C12N
001/20

Field of Search: 536/23.1,23.5,23.2
435/320.1,325,189,183,252.3,254.11,257.2

References Cited [Referenced By]

U.S. Patent Documents

<u>6013454</u>	Jan., 2000	Tang et al.	435/6.
<u>6207403</u>	Mar., 2001	Goldstein et al.	
<u>6410254</u>	Jun., 2002	Fiver et al.	

Other References

Pereira et al. (2000) "Mitochondrial association of a plus end-directed microtubule motor expressed during mitosis in Drosophila" J. Cell Biol. 136:1081-1090.

Wood et al. (1997) Genbank Accession #A97211. Direct Submission. S. pombe chromosome II cosmid c2F12.

Purnell et al. (1998) Genbank Accession #AL023587. Direct Submission, S. pombe Chromosome II cosmid c649.

Rieger et al. (1996) Genbank Accession #Z72739; Y3135. Direct Submission, S. cerevisiae chromosome VII.

Stewart et al. (1997) Genbank Accession #U89264. Direct Submission, Dm Kinesin-like protein 67a.

Primary Examiner: Duffy; Patricia A.

Attorney, Agent or Firm: Stevens; Lauren L. Beyer Weaver & Thomas, LLP

Claims

What is claimed is:

1. An isolated nucleic acid sequence encoding a motor protein, wherein the motor protein has the following properties: (i) the protein has microtubule stimulated ATPase activity; and (ii) the protein comprises a sequence that has greater than 90% sequence identity to SEQ ID NO:2 or SEQ ID NO:4 as measured using a sequence comparison algorithm.
2. An isolated nucleic acid sequence of claim 1, wherein the protein specifically binds to polyclonal antibodies to a protein comprising SEQ ID NO:2 or SEQ ID NO:4.
3. An isolated nucleic acid sequence, wherein the nucleic acid encodes a protein having an amino acid sequence comprising SEQ ID NO:2 or SEQ ID NO:4.
4. An isolated nucleic acid sequence having a nucleotide sequence comprising SEQ ID NO:1 or SEQ ID NO:3.
5. An isolated nucleic acid sequence of claim 1, wherein the nucleic acid sequence selectively hybridizes under high stringency conditions to a nucleic acid having a sequence or complementary sequence of SEQ ID NO:1 or SEQ ID NO:3, wherein said ***stringent hybridization*** conditions are selected from the group consisting of (1) 0.015 M sodium chloride/0.0015 M sodium citrate/0.1% sodium dodecyl sulfate at 50.degree. C.; (2) 50% formamide with 0.1% bovine serum albumin/0.1% Ficoll/0.1% polyvinylpyrrolidone/50 mM sodium phosphate buffer at pH 6.5 with 750 mM sodium chloride and 75 mM sodium citrate at 42.degree. C.; and (3) 50% formamide, 5.times.SSC (0.75 M sodium chloride, 0.75 M sodium citrate), 50 mM sodium phosphate (pH 6.8), 0.1% sodium pyrophosphate, 5.times.Denhardt's solution, 50 .mu.g/mL sonicated salmon sperm DNA, 0.1% sodium dodecyl sulfate and 10% dextran sulfate at 42.degree. C., with washes at 42.degree. C. in 0.2.times.SSC and 50% formamide at 55.degree. C., followed by a wash of 0.1.times.SSC containing EDTA at 55.degree. C.
6. An expression vector comprising a nucleic acid encoding a motor protein, wherein the motor protein has the following properties: (i) the protein has microtubule stimulated ATPase activity; and (ii) the protein comprises a sequence that has greater than 90% sequence identity to SEQ ID NO:2 or SEQ ID NO:4 as measured using a sequence comparison algorithm.

Gene encoding hyaluronan synthase

Abstract

An isolated and purified DNA molecule encoding hyaluronan synthase-2 (Has2) is provided, as is purified and isolated Has2 polypeptide.

Inventors: **McDonald; John A.** (Scottsdale, AZ); **Spicer; Andrew P.** (Scottsdale, AZ);
Augustine; Mary Louise (Scottsdale, AZ)

Assignee: **Clear Colutions Biotech, Inc.** (Stony Brook, NY)

Appl. No.: **675499**

Filed: **July 3, 1996**

Current U.S. Class: 435/183; 435/84; 435/252.3; 435/320.1; 435/325;
536/23.1; 536/23.2

Intern'l Class: C12N 009/00; C07H 021/04

Field of Search: 435/183,240.2,252.3,320.1,325,84 536/23.2,23.1
935/22

References Cited [Referenced By]

Other References

Hillier, L., et al., GenBank Accession No. W21505 "The WashU-Merck EST Project", [HTTP://www.ncbi.nlm.nih.gov](http://www.ncbi.nlm.nih.gov) unpublished (1995), 2, (1995).

Itano, N., et al., "Expression Cloning and Molecular Characterization of HAS Protein, a Eukaryotic Hyaluronan Synthase", The Journal of Biological Chemistry, vol. 271, No. 17, pp. 9875-9879, (Apr. 26, 1996).

McFall, A., et al., "Cell adhesion to the extracellular protein domain of syndecan-4", 6th Internat'l Congress on Cell Biology & 36th Amer. Soc. for Cell Biology Annual Meeting, Glycosaminoglycans and Proteoglycans I--Sunday, p. 326; (Dec. 7-11, 1996).

Semino, C.E., et al., "Homologs of the Xenopus developmental gene DG42 are present in zebrafish and mouse and are involved in the synthesis of nod-like chitin oligosaccharides during early embryogenesis", Proc. Natl. Acad. Sci. USA, vol. 93, , No. 10, pp. 4548-4553, (May 14, 1996).

Spicer, A.P., et al., "Molecular Cloning and Characterization of a Putative Mouse Hyaluronan Synthase", The Journal of Biological Chemistry, vol. 271, No. 38, pp. 23400-23406, (Sep. 20, 1996).

Spicer, A.P., et al., "Molecular cloning of a putative eukaryotic hyaluronan synthase, mHAS2", Sixth International Congress on Cell Biology & 36th Amer.

Society for Cell Biology Annual Meeting, p. 55a, (Dec. 7-11, 1996).

Watanabe, K., et al., "Molecular Identification of a Putative Human Hyaluronan Synthase", The Journal of Biological Chemistry, vol. 271, No. 38, pp. 22945-22948, (Sep. 20, 1996).

Itano et al. (1996) Molecular Cloning of Human Hyaluronan Synthase, Biochemical and Biophysical Research Communications 222: 816-820, Jun. 3, 1996.*

Rosa et al. (1988) Accumulation and Decay of DG42 Gene Products follow a Gradient Pattern During Xenopus Embryogenesis, Developmental Biology 129: 114-123, Feb. 1988.*

Ngo et al (1994) Computational Complexity, Protein Structure Prediction, and the Levinthal Paradox, Eds. Merz et al., Birkhauser, Boston, MA, pp. 433 and 492-495, Feb. 1994.*

R. K. Wilson, Nucleotide sequence, SW:DG42_Xenla P13563 DG42 Protein, dbEST Id. No.: 528557, GenBank Accession No.: W21505 (May, 1996).

P. L. DeAngelis, et al., "Immunochemical Confirmation of the Primary Structure of Streptococcal Hyaluronan Synthase and Synthesis of High Molecular Weight Product by the Recombinant Enzyme", Biochemistry, 33, 9033-9039 (Aug., 1994).

P. L. DeAngelis, et al., "Molecular Cloning, Identification, and Sequence of the Hyaluronan Synthase Gene from Group A Streptococcus pyogenes", J. Biol. Chem., 268, 19181-19184 (Sep., 1993).

N. Itano, et al., "Expression Cloning and Molecular Characterization of HAS Protein, a Eukaryotic Hyaluronan Synthase", J. Biol. Chem., 271, 9875-9878 (Apr., 1996).

M. F. Meyer, et al., "Cells Expressing the DG42 Gene from Early Xenopus Embryos Synthesize Hyaluronan", Proc. Natl. Acad. Sci., USA, 93, 4543-4547 (May, 1996).

C. E. Semino, et al., "Homologs of the Xenopus Developmental Gene DG42 are Present in Zebrafish and Mouse and Are Involved in the Synthesis of Nod-Like Chitin Oligosaccharides During Early Embryogenesis", Proc. Natl. Acad. Sci., USA, 93, 4548-4553 (May, 1996).

A. Varki, "Does DG42 Synthesize Hyaluronan or Chitin?: A Controversy About Oligosaccharides in Vertebrate Development", Proc. Natl. Acad. Sci., USA, 93, 4523-4225 (May, 1996).

Primary Examiner: Prouty; Rebecca E.

Assistant Examiner: Hutson; Richard

Claims

What is claimed is:

1. An isolated and purified DNA molecule comprising a DNA segment encoding a

mammalian hyaluronan synthase or an enzymatically active fragment thereof, wherein the DNA molecule hybridizes under *stringent hybridization* conditions to the DNA molecule having SEQ ID NO:1 or the complement thereof.

2. An expression cassette comprising a promoter operably linked to the DNA molecule of claim 1.

3. A host cell transformed with the DNA molecule of claim 1.

4. A method to produce hyaluronan synthase, comprising: culturing a host cell transformed with the DNA molecule of claim 1 operably linked to a promoter, so that said host cell expresses recombinant hyaluronan synthase.

5. The method of claim 4 further comprising isolating said hyaluronan synthase from the host cell.

6. A method of altering the amount of hyaluronan produced by a cell, comprising:

(a) introducing into a host cell the DNA molecule of claim 1 operably linked to a promoter functional in the host cell so as to yield a transformed host cell; and

(b) expressing the DNA segment in the transformed host cell in an amount that alters the amount of hyaluronan produced by the transformed cell relative to the amount of hyaluronan produced by a corresponding untransformed cell.

7. The method of claim 6 wherein the amount of hyaluronan produced by the transformed host cell is increased relative to the amount of hyaluronan produced by the corresponding untransformed host cell.

8. The method of claim 6 wherein the amount of hyaluronan produced by the transformed host cell is decreased relative to the amount of hyaluronan produced by the corresponding untransformed host cell.

9. The DNA molecule of claim 1 wherein the DNA segment encodes murine hyaluronan synthase.

10. The DNA molecule of claim 9 or 1 wherein the DNA segment encodes the hyaluronan synthase having SEQ ID NO:2.

11. The DNA molecule of claim 1 wherein the DNA segment comprises SEQ ID NO:1.

12. The DNA molecule of claim 1 wherein the DNA segment encodes human hyaluronan synthase.

13. The DNA molecule of claim 12 or 1 wherein the DNA segment comprises SEQ ID NO:23.

Nucleic acid molecules encoding CASPR/p190

Abstract

The 190 kDa Contactin ASSociated PRotein (CASPR/p190) is identified and is implicated as the bridge between contactin and intracellular second messenger systems for the signal caused by the binding of the carboxy anhydrase domain of RPTP.beta. to contactin and resulting in neurite growth, differentiation or survival. Mammalian CASPR/p190 cDNAs and proteins are described, including those from human and rat. In addition, particular domains of the proteins are characterized.

Inventors: **Peles; Elior** (Foster City, CA)

Assignee: **Sugen, Inc.** (South San Francisco, CA)

Appl. No.: **826134**

Filed: **March 26, 1997**

Current U.S. Class: 435/69.1; 435/70.1; 435/71.1; 435/71.2; 435/243;
435/252.3; 435/254.2; 435/320.1; 435/325; 536/23.5

Intern'l Class: C07H 021/04; C12N 015/00; C12N 001/20; C12P
021/04

Field of Search: 536/23.1,23.5
435/69.1,70.1,71.1,71.2,325,243,252.3,320.1,254.2

References Cited [Referenced By]

Other References

- Bare et al., 1993, "p59.sup.fyn in Rat Brain is Localized in Developing Axonal Tracts and Subpopulations of Adult Neuron and Glia", *Oncogene* 8:1429-1436.
- Barnea et al., 1993, "Close Similarity Between Receptor-Linked Tyrosine Phosphatase and Rat Brain Proteoglycan", *Cell* 76:205.
- Barnea et al., 1994, "Receptor Tyrosine Phosphatase .beta. is Expressed in the Form of Proteoglycan and Binds to the Extracellular Matrix Protein Tenascin", *J. Biol. Chem.* 269:14349-14352.
- Barnea et al., 1993, "Identification of a Carbonic Anhydrase-Like Domain in the Extracellular Region of RPTP.gamma. Defines a New Subfamily of Receptor Tyrosine Phosphatases", *Mol. Cell. Biol.* 13:1497-1506.
- Beggs et al., 1993, "NCAM-Dependent Neurite Outgrowth is Inhibited in Neurons from fyn-Minus Mice", *J. Cell. Biol.* 127:825-833.
- Berglund and Ranscht, 1994, "Molecular Cloning and in situ Localization of the Human Contactin Gene (CNTN1) on Chromosome 12q11-q12", *Genomics*

Wolff, J.M., F.G. Rathjen, and S. Roth. 1987. Biochemical characterization of polypeptide components involved in neurite fasciculation and elongation. Eur. J. Biochem. 168:551-561.

Primary Examiner: Duffy; Patricia A.
Attorney, Agent or Firm: Foley & Lardner

Parent Case Text

The present application claims priority under 35 U.S. .sectn. 119(e) to provisional application Ser. No. 60/014,199, filed Mar. 27, 1996, the entire contents of which is incorporated herein by reference in its entirety.

Claims

What is claimed is:

1. An isolated nucleic acid molecule comprising a nucleotide sequence that:
 - (a) encodes the amino acid sequence SEQ ID NO:2; or
 - (b) encodes the amino acid sequence SEQ ID NO:4.
2. An isolated nucleic acid molecule comprising a nucleotide sequence that hybridizes under highly stringent conditions to the full complement of the nucleic acid molecule of claim 1, and encodes a naturally occurring p190 polypeptide, wherein the highly ***stringent hybridization*** conditions comprise washing in 0.1.times.SSC/0.1% SDS at 68.degree. C.
3. An isolated nucleic acid molecule which comprises (a) a nucleotide sequence that encodes a polypeptide having the amino acid sequence shown in SEQ ID NO:2 from amino acid residues 40-168, 199-330, 362-486, 544-576, 582-739, 809-938, 961-985, 1031-1077, 1083-1218, or 1328-1369; or (b) a nucleotide sequence that is fully complementary to the nucleotide sequence of (a).
4. An isolated nucleic acid molecule which comprises
 - (a) a nucleotide sequence that encodes a p190 polypeptide lacking at least one, but not all, of the following segments of amino acid residues: 40-168, 199-330, 362-486, 544-576, 582-739, 809-938, 961-985, 1031-1077, 1083-1218, 1282-1306, or 1328-1369 of SEQ ID NO:2; or;

Papilloma viruses, products for the detection thereof as well as for treating diseases caused by them

Abstract

This invention relates to a DNA coding for a peptide of a papilloma virus major capsid protein and a papilloma virus genome, respectively. Furthermore, this invention concerns proteins coded by the papilloma virus genome and antibodies directed thereagainst as well as the use thereof for diagnosis, treatment and vaccination.

Inventors: **De Villiers-Zur Hausen; Ethel-Michele (Waldmichelbach, DE); Zur Hausen; Harald (Waldmichelbach, DE); Lavergne; Donna (Florsheim/Dalsheim, DE); Benton; Claire (Edinburgh, GB)**
Assignee: **Deutsches Krebsforschungszentrum Stiftung des Offentlichen Rechts (Heidelberg, DE)**
Appl. No.: **319056**
Filed: **August 5, 1999**
PCT Filed: **November 12, 1997**
PCT NO: **PCT/DE97/02659**
371 Date: **August 5, 1999**
102(e) Date: **August 5, 1999**
PCT PUB.NO.: **WO98/23752**
PCT PUB. Date: **June 4, 1998**

Foreign Application Priority Data

Nov 26, 1996[DE]

196 48 962

Current U.S. Class: 424/204.1; 424/199.1; 435/5; 435/69.1; 435/69.3; 435/235.1; 435/320.1; 536/23.72; 530/350; 530/324
Intern'l Class: A61K 039/12; C12N 001/12; C12N 015/00; C07H 021/04
Field of Search: 435/6,701,69.3,69.1,235.1,320.1 536/23.1,23.72 396/2,1 530/350,387.1,324 424/204.1,199.1

References Cited [Referenced By]

Foreign Patent Documents

WO 95/30754	Nov., 1995	WO.
WO 97/04099	Feb., 1997	WO.

Other References

de Villiers et al., 1997, "Prevailing papillomaviruses types in non-melanoma carcinomas of the skin in renal allograft recipients," *International Journal of Cancer* 73(3):356-361.
Hagensee et al., 1993, "Self-assembly of human papillomavirus type 1 capsids by expression of the L1 protein alone or by coexpression of the L1 and L2 capsid proteins," *Journal of Virology* 67(1):315-322.
Kirnbauer et al., 1993, "Efficient self-assembly of human papillomavirus type 16 L1 and L2 into virus-like particles," *Journal of Virology* 67(12):6929-6936.
zur Hausen, 1977, "Human papillomavirus and their possible role in squamous cell carcinomas," *Curr. Top. Microbiol. Immunol.* 78:1-30.
zur Hausen, 1996, "Papillomavirus infections--a major cause of human cancers," *Biochimica et Biophysica Acta* 1288(2):F55-F78.

Primary Examiner: Salimi; Ali R.

Attorney, Agent or Firm: Pennie & Edmonds LLP

Parent Case Text

This is a national phase filing of the Application No. PCT/DE97/02659, which was filed with the Patent Corporation Treaty on Nov. 12, 1997, and is entitled to priority of the German Patent Application DE 196 48 962.8, filed Nov. 26, 1996.

Claims

What is claimed is:

1. An isolated polynucleotide consisting essentially of:

(a) a nucleotide sequence encoding the peptide of SEQ ID NO:2, SEQ ID NO:5, or SEQ ID NO:8;

(b) a nucleotide sequence hybridizing to the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:4, or SEQ ID NO:7; or

(c) the complement of (a) or (b);

wherein the polynucleotide has a homology of at least 90% to the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:4, or SEQ ID NO:7, or the complement thereof.

2. An isolated polynucleotide encoding a peptide of a papilloma virus major capsid protein, wherein the said polynucleotide has been obtained using the following steps:

(a) incubating total DNA isolated from a biopsy of epithelial neoplasm with a nucleic acid having at least a portion of the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:4, or SEQ ID NO:7, under a condition that allows hybridization of a polynucleotide derived from a papilloma virus genome included in the total DNA to said nucleotide sequence of the complement of SEQ ID NO:1, SEQ ID NO:4, or SEQ ID NO:7; and

(b) identifying and isolating a polynucleotide that hybridizes to the complement of the nucleotide

sequence of SEQ ID NO:1, SEQ ID NO:4, or SEQ ID NO:7 in step (a);

wherein the polynucleotide has a homology of at least 90% to the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:4, or SEQ ID NO:7.

3. An isolated polynucleotide, consisting essentially of (a) a nucleic acid encoding a peptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:5, or SEQ ID NO:8, or (b) the complement of (a).

4. An isolated polynucleotide, wherein the polynucleotide consists essentially of the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:4, or SEQ ID NO:7, or the complement thereof.

5. A plasmid comprising the polynucleotide of claim 1 or 2.

6. A plasmid comprising the polynucleotide of claim 3 or 4.

7. An expression vector comprising the polynucleotide of claim 1 or 2.

8. An expression vector comprising the polynucleotide of claim 3 or 4.

9. A host cell comprising the plasmid of claim 5.

10. A host cell comprising the plasmid of claim 6.

11. A host cell comprising the expression vector of claim 9.

12. A host cell comprising the expression vector of claim 8.

13. A method of producing a peptide of a papilloma virus major capsid protein, comprising cultivating the host cell of claim 11 under suitable conditions.

14. A method of producing a peptide of a papilloma virus major capsid protein, comprising cultivating the host cell of claim 12 under suitable conditions.

15. A method of detecting a papilloma virus DNA, comprising:

(a) **hybridizing under stringent conditions** at least a portion of the polynucleotide of claim 1, 2, 3, or 4 to a DNA sample; and

(b) identifying papilloma virus in said DNA sample by detecting a hybridization signal.

16. A composition comprising the polynucleotide of claim 1, 2, 3, or 4 as reagent for diagnosis and a diagnostically acceptable carrier.

17. A method of producing a papilloma virus genome, comprising:

(a) incubating total DNA isolated from a biopsy of epithelial neoplasm with a nucleic acid having at least a portion of the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:4, or SEQ ID NO:7, under a condition that allows hybridization of a polynucleotide derived from a papilloma virus genome included in the total DNA to said nucleotide sequence of the complement of SEQ ID NO:1, SEQ ID NO:4, or SEQ ID NO:7; and

United States Patent
Quandt, et al.

6,384,304
May 7, 2002

Conditional sterility in wheat

Abstract

The invention relates to the use of a deacetylase coding sequence for obtaining conditional sterility in wheat. The invention relates to vectors comprising a deacetylase coding sequence under control of promoters which direct stamen-selective expression in wheat, which are particularly suited for the production of wheat plants which can be made male-sterile upon application of an acetylated toxin.

Inventors: **Quandt; Jurgen** (Saskatoon, CA); **Bartsch; Klaus** (Konigstein, DE); **Knittel; Nathalie** (Frankfurt, DE)

Assignee: **Plant Genetic Systems N.V.** (Gent, BE)

Appl. No.: **418817**

Filed: **October 15, 1999**

Current U.S. Class: 800/320.3; 435/418; 435/419; 435/468; 800/271; 800/274; 800/278; 800/287; 800/288; 800/300; 800/303

Intern'l Class: C12N 015/82; C12N 015/31; C12N 005/04; A01H 005/00; A01H 001/02

Field of Search: 800/320.3,288,300,287,274,303,271,278 435/418,419,468

References Cited [Referenced By]

U.S. Patent Documents

<u>5633441</u>	May., 1997	DeGreef et al.	800/205.
<u>5650310</u>	Jul., 1997	Broer et al.	435/172.
<u>5668297</u>	Sep., 1997	Broer et al.	800/205.
<u>5689041</u>	Nov., 1997	Mariani et al.	800/205.
<u>5723763</u>	Mar., 1998	Mariani et al.	800/205.
<u>5767370</u>	Jun., 1998	Broer et al.	800/205.
<u>5767371</u>	Jun., 1998	Broer et al.	800/205.
<u>5767374</u>	Jun., 1998	DeGreef et al.	800/205.
<u>5792929</u>	Aug., 1998	Mariani et al.	800/205.
<u>5981189</u>	Nov., 1999	Chan et al.	435/6.
<u>6177616</u>	Jan., 2001	Bartsch et al.	800/303.

Foreign Patent Documents

344029	Nov., 1989	EP.
WO 98/13504	Apr., 1998	WO.
WO 98/27201	Jun., 1998	WO.
WO 98/39462	Sep., 1998	WO.

Other References

Kriete G. et al., "Male sterility in transgenic tobacco plants induced by tapetum-specific deacetylation of the externally applied non-toxic compound N-acetyl-L-phosphinothricin." 1996, The Plant Journal, vol. 9, pp. 809-818.*

"The development of a nuclear male sterility system in wheat. Expression of the barnase gene under the control of tapetum specific promoters"; DeBlock et al., 1997, Theor. Genet. 95: 125-131.

Primary Examiner: Fox; David T.

Attorney, Agent or Firm: Frommer Lawrence & Haug LLP

Claims

We claim:

1. A wheat plant, having a chimeric gene integrated into its genome, the chimeric gene comprising:
 - a) a DNA molecule encoding a deacetylase from *Stenotrophomonas* sp; and
 - b) a promoter directing stamen-selective expression in wheat wherein the DNA molecule encoding the deacetylase is in the same transcriptional unit and under control of the stamen-selective promoter.
2. The wheat plant of claim 1, wherein said DNA molecule encodes a biologically active fragment or a variant of the deacetylase encoded by SEQ ID No. 9.
3. The wheat plant of claim 1, wherein said DNA molecule encodes a deacetylase having the amino acid sequence of SEQ ID No. 8.
4. The wheat plant of claim 1, wherein said DNA molecule comprises the sequence of SEQ ID No. 9, or a sequence capable of hybridizing to SEQ ID No. 9 under standard *stringent* conditions.
5. The wheat plant of claim 1, wherein said stamen-selective promoter is a CA55 promoter.
6. The wheat plant of claim 1, wherein said stamen-selective promoter is a T72 promoter.
7. The wheat plant of claim 1, wherein said stamen-selective promoter is an E1 promoter.
8. A process for producing *hybrid* wheat seed, said process comprising
 - i) producing seeds capable of growing into conditionally male-sterile wheat plants, said seeds having a chimeric gene integrated in their genome, the chimeric gene comprising:
 - a) a DNA molecule encoding a deacetylase from *Stenotrophomonas* sp., and
 - b) a stamen-selective promoter wherein the DNA molecule encoding the deacetylase is in the same transcriptional unit and under the control of the stamen-selective promoter;

ii) interplanting said seeds capable of growing into conditionally male-sterile wheat plants with seeds capable of growing into male fertile wheat plants;

iii) inducing male-sterility in said conditionally male-sterile plants by applying an N-acetyl-PPT, which in itself is not toxic to the plants or plant cells; and

iv) harvesting *hybrid* seed.

9. The process of claim 8, wherein said DNA molecule encodes a biologically active fragment or a variant of the deacetylase encoded by SEQ. ID. No. 9.

10. The process of claim 8, wherein said DNA molecule encodes the deacetylase comprising the amino acid sequence of SEQ ID No. 8.

11. The process of claim 8, wherein said DNA molecule comprises the sequence of SEQ ID No. 9, or a sequence capable of hybridizing to SEQ ID No. 9 under standard *stringent* conditions.

12. The process of claim 8, wherein said stamen-selective promoter is a CA55 promoter.

13. The process of claim 8, wherein said stamen-selective promoter is a T72 promoter.

14. The process of claim 8, wherein said stamen-selective promoter is an E1 promoter.

15. The process of claim 8, wherein said male fertile plants are female-sterile.

16. A process for producing a conditionally male-sterile wheat plant, said process comprising

i) transforming a wheat plant cell or tissue with a chimeric gene which comprises:

a) a DNA molecule encoding a deacetylase from *Stenotrophomonas* sp., and

b) a stamen-selective promoter wherein the DNA molecule encoding the deacetylase is in the same transcriptional unit and under the control of said stamen-selective promoter;

ii) regenerating said conditionally male-sterile plant from said cell or tissue; and optionally,

iii) applying an N-acetyl-PPT to said conditionally male-sterile plant, which is in itself not toxic to the plant or plant cells to make said plant male-sterile.

17. The process of claim 16, wherein said DNA molecule encodes a biologically active fragment of the deacetylase encoded by SEQ. ID. No. 9.

18. The process of claim 16, wherein said DNA molecule encodes the deacetylase of SEQ ID No. 8.

19. The process of claim 16, wherein said DNA molecule comprises the sequence of SEQ ID No. 9, or a sequence capable of hybridizing to SEQ ID No. 9 under standard *stringent* conditions.

20. The process of claim 16, wherein said stamen-selective promoter is a CA55 promoter.

21. The process of claim 16, wherein said stamen-selective promoter is a T72 promoter.

Seed specific promoters

Abstract

The present invention is directed to isolated promoter sequences from seed-specific genes, such as KNAT411. When operably linked to either the coding sequence of a heterologous gene or a sequence complementary to a native plant gene, the subject promoters direct expression of the coding sequence or complementary sequence in a plant seed, including the early embryo. The promoter sequences are useful in expression cassettes and expression vectors for the transformation of plants. Also provided are methods of directing seed-specific expression of a gene or sequence complementary to a native plant gene by introducing into a plant cell an isolated nucleic acid comprising a subject promoter operably linked to said gene or complementary sequence. Methods for activating a site-specific recombination system in the early embryo of a seed by transforming a plant with an expression cassette comprising a subject promoter operably linked to a recombinase gene are also provided.

Inventors: **Thomas; Terry L.** (College Station, TX); **Hsieh; Tzung-Fu** (College Station, TX)

Assignee: **Rhone-Poulenc Agro** (Lyons, FR)

Appl. No.: **306060**

Filed: **May 6, 1999**

Current U.S. Class: 800/287; 435/69.1; 435/320.1; 435/419; 435/468; 435/471;
536/24.1; 800/281; 800/298; 800/306; 800/312; 800/314;
800/320.1; 800/322

Intern'l Class: C12N 005/04; C12N 015/82; C12N 015/90; A01H 005/00;
A01H 005/10

Field of Search: 435/69.1,320.1,410,412,415,416,414,419,468
536/23.6,24.1
800/278,281,286,287,295,298,306,312,314,317.3,320.1,322

References Cited [Referenced By]

Foreign Patent Documents

WO 98/45461	Oct., 1998	WO
WO 99/20775	Apr., 1999	WO

Other References

Baumlein et al, Mol. Gen. Genet., vol. 225, pp. 459-467, 1991.*

Kerstetter, R., et al. (1994) "Sequence Analysis and Expression Patterns Divide the Maize knotted1-like Homeobox Genes into Two Classes" The Plant Cell 6: 1877-1887.

Long, J., et al. (1996) "A member of the knotted class of homeodomain proteins encoded by the STM gene of Arabidopsis" Nature 379: 66-69.

Cartea, M. E., et al. (1998) "Comparison of sense and antisense methodologies for modifying the fatty acid composition of Arabidopsis thaliana oilseed " Plant Science 136: 181-194.

Odell, J., et al. (1994) "Seed-Specific Gene Activation Mediated by the Cre/lox Site-Specific Recombination System" Plant Physiol 106: 447-458.

Primary Examiner: Benzion; Gary

Assistant Examiner: Mehta; Ashwin

Attorney, Agent or Firm: Scully, Scott, Murphy & Presser

Claims

What is claimed is:

1. An isolated nucleic acid comprising a promoter which has the seed-specific promoter activity of the KNAT411 promoter, said promoter hybridizing under ***stringent hybridization*** conditions to the KNAT411 promoter having the nucleotide sequence as set forth in SEQ ID NO:1, wherein said ***stringent hybridization*** conditions comprise hybridization in 4.times.SSC at 65.degree. C. and washing in 0.1.times.SSC at 65.degree. C.
2. An isolated nucleic acid comprising a promoter which has the seed-specific promoter activity of the KNAT411 promoter, said promoter having a sequence identity of about 60% to about 65% when compared to the nucleotide sequence of the KNAT411 promoter as set forth in SEQ ID NO:1.
3. An isolated nucleic acid comprising a promoter which has the seed-specific promoter activity of the KNAT411 promoter, said promoter having a sequence identity of about 65% to about 75% when compared to the nucleotide sequence of the KNAT411 promoter as set forth in SEQ ID NO:1.
4. An isolated nucleic acid comprising a promoter which has the seed-specific promoter activity of the KNAT411 promoter, said promoter having a sequence identity of about 75% to about 85% when compared to the nucleotide sequence of the KNAT411 promoter as set forth in SEQ ID NO:1.
5. An isolated nucleic acid comprising a promoter which has the seed-specific promoter

United States Patent
Kunst, et al.

6,274,790
August 14, 2001

Nucleic acids encoding a plant enzyme involved in very long chain fatty acid synthesis

Abstract

Nucleic acid molecules encoding an enzyme involved in very long chain fatty acid (VLCFA) elongation in plants are disclosed. The invention includes a cDNA, genomic clone and encoded protein, as well as plants having modified VLCFA composition, such as modified epicuticular waxes, and methods of making such plants.

Inventors: **Kunst; Ljerka** (North Vancouver, CA); **Millar; Anthony A.** (Vancouver, CA)

Assignee: **The University of British Columbia** (Vancouver, CA)

Appl. No.: **058947**

Filed: **April 10, 1998**

Current U.S. Class: 800/287; 435/468; 536/24.1; 800/281; 800/298

Intern'l Class: C12N 015/82; A01H 005/00; C07H 021/04

Field of Search: 800/298,281,264,287 435/69.1,468,419,430,320.1 536/23.6

References Cited [Referenced By]

U.S. Patent Documents

<u>5443974</u>	Aug., 1995	Hitz et al.
<u>5455167</u>	Oct., 1995	Voelker et al.
<u>5530192</u>	Jun., 1996	Murase et al.

Foreign Patent Documents

4433307A	Mar., 1996	DE.
WO95/15387	Jun., 1995	WO.
WO96/13582	May., 1996	WO.

Other References

Benfey et al., Science 250:959-966, Nov. 1990.*

Newman et al., "AC T22193," EMBL Database, Jun. 27, 1994.

Newman et al., "AC T76616," EMBL Database, Mar. 25, 1995.

Sohal & Jenkins, "Epidermal-specific gene expression in Brassica and Arabidopsis," Plant Physiology Supplement, vol. 111, No. 2, p. 6, Jun. 2, 1996.

Evenson & Post-Beittenmiller, "Fatty acid-elongation activity in rapidly expanding leek epidermis," Plant Physiology, vol. 109, pp. 707-716, 1995.

Millar & Kunst, "Very-long-chain fatty acid biosynthesis is controlled through the expression and specificity of the condensing enzyme" The Plant Journal 12(1):121-131, 1997.

Newman et al., "Genes Galore: A Summary of Methods for Accessing Results from Large-

Scale Partial Sequencing of Anonymous Arabidopsis cDNA Clones" Plant Physiol., 106:1241-1255, 1994.

Katavic et al., "In planta transformation of Arabidopsis thaliana " Mol Gen Genet, 245:363-370, 1994.

Lemieux, "Molecular genetics of epicuticular wax biosynthesis" Trends in Plant Science, 1 (9):312-318, 1996.

Kunst et al., "Fatty acid elongation in developing seeds of Arabidopsis thaliana" Plant Physiol. Biochem., 30:(4) 425-434, 1992.

Lassner et al., "A Jojoba .beta.-Ketoacyl-CoA Synthase cDNA Complements the Canola Fatty Acid Elongation Mutation in Transgenic Plants" The Plant Cell, 8:281-292, 1996.

James et al., "Directed Tagging of the Arabidopsis Fatty Acid Elongation 1 (FAE1) Gene with the Maize Transposon Activator," The Plant Cell, 7:309-319, 1995.

James & Dooner, "Isolation of EMS-induced mutants in Arabidopsis altered in seed fatty acid composition" Theor Appl Genet, 80:241-245, 1990.

Lemieux et al., "Mutants of Arabidopsis with alterations in seed lipid fatty acid composition" Theor Appl Genet, 80:234-240, 1990.

Primary Examiner: McElwain; Elizabeth F.

Attorney, Agent or Firm: Klarquist Sparkman Campbell Leigh & Whinston, LLP

Parent Case Text

PRIORITY CLAIM

This application claims priority to co-pending U.S. provisional patent application Ser. No. 60/043,831, filed on Apr. 14, 1997.

Claims

We claim:

1. A recombinant nucleic acid molecule comprising a promoter sequence operably linked to a nucleic acid sequence, wherein the promoter sequence comprises a transcriptional regulatory region capable of mediating gene expression in epidermal cells of Arabidopsis wherein the transcriptional regulatory region hybridizes under stringent conditions to: Seq. I.D. No. 12 or the complement of Seq. I.D. No. 12.
2. A recombinant nucleic acid molecule according to claim 1 wherein the promoter sequence comprises at least 50 consecutive nucleotides of the sequence shown in Seq. I.D. No. 12 or the complement of Seq. I.D. No. 12.
3. The recombinant nucleic acid molecule according to claim 1, wherein the promoter sequence is at least 70% identical to the sequence set forth in Seq. I.D. No. 12.
4. A recombinant nucleic acid molecule according to claim 1, wherein the promoter sequence is at least 80% identical with the sequence set forth in Seq. I.D. No. 12 or the complement of Seq. I.D. No. 12.

5. A recombinant vector comprising a nucleic acid molecule according to claim 1.
6. A transgenic plant comprising a heterologous nucleic acid sequence, wherein the heterologous nucleic acid sequence comprises the recombinant nucleic acid molecule of claim 1.
7. The recombinant nucleic acid molecule according to claim 1, wherein the nucleic acid sequence encodes a protein having very long chain fatty acid elongase activity.
8. A method of producing a transgenic plant comprising introducing into the plant the recombinant nucleic acid molecule of claim 1.
9. A plant produced by sexual or asexual propagation of the transgenic plant produced according to the method of claim 8, or by propagation of progeny of the transgenic plant, wherein the plant comprises the recombinant nucleic acid molecule.
10. A method of isolating a nucleic acid molecule having promoter activity, comprising *hybridizing under stringent conditions* a nucleic acid preparation with a probe comprising Seq. I.D. No. 12 or the complement of Seq. I.D. No. 12.
11. A plant cell comprising a heterologous nucleic acid sequence, wherein the heterologous nucleic acid sequence comprises the recombinant nucleic acid molecule of claim 1.
12. A recombinant nucleic acid molecule comprising a promoter sequence operably linked to a nucleic acid sequence, wherein the promoter sequence comprises a transcriptional regulatory region capable of mediating gene expression in epidermal cells of Arabidopsis wherein the transcriptional regulatory region is obtainable from a plant VLCFA condensing enzyme gene comprising an open reading frame that hybridizes under stringent conditions to Seq. I.D. No. 3 or to the complement of Seq. I.D. No. 3.